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PRINCIPAL INVESTIGATOR: Joseph R. Calabrese, M.D.

CONTRACTING ORGANIZATION: University Hospitals of Cleveland
Cleveland, OH 44106-5000

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14. ABSTRACT The general objective of the Combat Mental Health Initiative is to create a research infrastructure capable of supporting a series of projects that evaluate the relationships between resilience and risk factors, both cross-sectionally and longitudinally, before, during, and after deployment. The primary project will collect long-term data on a random representative sample of 3,000 service members of the Ohio National Guard, both treatment seeking and non-treatment seeking. Research visits will be conducted at study entry, every 12 months for a minimum of 10 years, and 90-180days post-deployment. The key accomplishments of this project to date focus on the establishment of solid, mutually beneficial working relationships with the leadership of the Ohio National Guard and the creation of a six site research infrastructure necessary to carry out the projects' short-and long-term objectives. This project will provide the military with novel, landmark long-term, prospective data that will elucidate novel predictors of resilience to combat-related stress. Compared to existing research in this area, this project is unique because it is population-based and does not limit its scope of study to only VA-treatment seeking veterans. Accordingly, this study is likely to uncover rates of PTSD and other mental conditions following combat that differ from those found in previous scientific reports.					
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Combat Mental Health Initiative

**Risk and Resilience Factors for Combat-Related Posttraumatic Psychopathology and
Post Combat Adjustment**

First Annual Report, June 2008

Table of Contents

	<u>Page</u>
Introduction.....	4
Body.....	4 - 7
Key Research Accomplishments.....	7
Reportable Outcomes.....	7
Conclusion.....	7
References.....	8
Appendices.....	8 - 9

Combat Mental Health Initiative

Risk and Resilience Factors for Combat-Related Posttraumatic Psychopathology and Post Combat Adjustment

First Annual Report, June 2008

INTRODUCTION

Previously conducted research has demonstrated that deployment accompanied by combat experience results in increased risk of posttraumatic psychopathology and other mental health conditions. The general objective of the Combat Mental Health Initiative is to create a research infrastructure capable of supporting a series of projects that evaluate the relationships between resilience and risk factors, both cross-sectionally and longitudinally, before, during, and after deployment. The primary project will collect long-term data on a random representative sample of 3,000 service members of the Ohio National Guard, both treatment seeking and non-treatment seeking. Research visits will be conducted at study entry, every 12 months for a minimum of 10 years, and 90-180 days post-deployment.

BODY

The team of individuals and infrastructures committed to this project is extensive and has a reporting relationship to the leadership of the Ohio National Guard, Adjutant General Wayt and COL John Harris, through the Guard's OHIOCARES Group. The Principal Investigator (PI) of the Combat Mental Health Initiative is Joseph R. Calabrese, M.D. and the Co-PI is Marijo Tamburrino, M.D. The Initiative includes a Coordinating Center based out of University Hospitals Case Medical Center (UHCMC) (Dr. Calabrese), and six operating research sites including University Hospitals Case Medical Center, the University of Toledo (Dr. Tamburrino), the University of Michigan Department of Epidemiology (Dr. Galea), a prestigious research survey firm, Abt SRBI, Inc. with a very long history of military research, the Ann Arbor VAMC Department of Psychiatry at the University of Michigan (Dr. Liberzon), and Michigan State University's Biomedical Research and Informatics Center - BRIC (Dr. Reed).

With Dr. Calabrese as the coordinating principal investigator, the UHCMC is responsible for all aspects of project coordination (scientific, administrative, and fiscal) and the conduct of in-person assessments of 250 service members in their local communities. With Dr. Tamburrino as project Co-PI, the University of Toledo provides leadership and also conducts in-person assessments of 250 service members in their local communities. The University of Michigan Department of Epidemiology responsibilities include, but are not be limited to, the design of the project's field procedures, including the telephone survey and in-person validation sub-sample, scientific manuscript preparation, NIMH grant application, etc. Dr. Galea also serves as the primary interface between the project and the survey firm, Abt SRBI, which carries out the telephone surveys. The University of Michigan Ann Arbor VA Department of Psychiatry is responsible for the design, implementation, and oversight of the Genetics Repository, including laboratory and field procedures for biological sample collection, processing, storage, association analyses, etc. The Michigan State University Biomedical Research Informatics Center will provide all aspects of data management needs for the in-person validation sub-sample assessments (500 service members per year for 10 years),

including data entry and management privileges, enrolment privileges, survey building privileges, etc.

The Initiative is overseen by the leadership of the Ohio National Guard, the Office of Congresswoman Marcy Kaptur, the Military Operational Medicine Research Program, and more recently, the Telemedicine and Advanced Technologies Research Center. The confirmed membership of the project's External Scientific Advisory Board will meet to review preliminary findings during the first quarter of 2009 and the confirmed membership of the project's Administrative Advisory Board will do so during the second quarter.

The primary project within this initiative is a population-based clinical epidemiology and health services project and is designed to function as the template, upon which other projects, including but not limited to those of a translational research nature. The first four specific aims of the primary research project were designed to build support and stimulate additional interest in the study of the role of risk and resilience in combat-related posttraumatic psychopathology and other similar adjustment problems. The fifth specific aim of this project is to obtain permission to re-contact previously studied, well-characterized research subjects and their family members for future research that specifically targets the improvement of the scientific understanding of combat-related posttraumatic psychopathology and similar adjustment problems.

Specific Aims:

1. To Study the Promotion of Resilience to Combat-Related Stress
2. To Study the Effect of Deployment on DSM-IV Axis I Diagnoses
3. To Study the Effect of Combat Experience on Post-Deployment Function
4. To Study the Effect of Family Psychiatric History on Posttraumatic Psychopathology Following Deployment

The is designed to study the relationships between 1) pre-existing mental illness/substance use disorders, 2) deployment to Operation Iraqi Freedom (OIF) or Operation Enduring Freedom (OEF), and 3) post-deployment related mental health and overall psychosocial adjustment and functioning. The study will evaluate several groups of the Ohio National Guard: those deployed to OIF (Iraq, Kuwait, or Qatar), those deployed OEF (Afghanistan), those deployed to other theaters (Bosnia, Turkey, Uzbekistan, Kosovo, on a ship, or other), those deployed domestically, and those not deployed.

This project will enroll up to 3,000 members of the Ohio National Guard, who will be selected at random from the entire population of the Guard. All individuals who participate will be interviewed for 1 hour by telephone beginning during the summer of 2008 (telephone survey).

A validation sub-sample of 500 participants of the telephone survey group will also be invited to participate in an in-person interview, which will last 2-3 hours. This sub-sample will allow both for validation of key domains employed in the phone/web interviews and for further study of trajectory of psychopathology in this sample. Study personnel will recommend that participants bring a family member, friend, or significant other for support and assistance during the interview. Family support often facilitates participant retention throughout the life of the project.

We anticipate obtaining a random representative sample of National Guard members that will have variable lengths of involvement and combat exposures, allowing us to adequately address the proposed aims.

Research visits will be conducted at study entry, every 12 months for a minimum of 10 years, and 90-180 days post-deployment if applicable for both the telephone survey and in person survey. We anticipate that we will sample National Guard service members that have variable lengths of involvement and variable combat exposures, allowing us to suitably address the specific aims.

After the genetic's addendum to the primary project is reviewed and approved (addendum submission planned for the second half of 2008), all of those participating in the primary project will also have the opportunity to participate in the genetics repository. The "Genetics of Risk and Resilience for Deployment Related Stress Disorders" project will be led by Israel Liberzon, MD at the Ann Arbor VAMC. This first translational project will involve the creation of a DNA repository, which will be used to perform genetic association studies on selected candidate alleles and potentially genome-wide analyses at multiple levels. These may include cross-sectional genetic association analyses of pre-deployment traits, longitudinal analyses to investigate genetic markers and functional polymorphisms involved in vulnerability to deployment-related psychiatric disorders (i.e. in case-control association analyses), as well as building models incorporating measures of deployment-related and pre-deployment environmental factors for vulnerability (i.e. gene x environment interactions). This will also allow for integrated research utilizing neuroimaging, psychophysiological, and neuroendocrine measures to investigate the effects of genetic variants on cognitive, behavioral, and physiological function at baseline and after deployment stressors.

Progress to Date

The first 36 months of this research 10 year project have been funded by the DoD through FY 06, 07, and 08 awards totaling \$9.9 million. The primary project has required extensive initial interactions and approvals. This preliminary work has been of strategic importance and has resulted in a strong scientifically rigorous virtual research infrastructure overseen by the Office of Research Protections at USAMRMC, the office of Congresswoman Marcy Kaptur, and the institutional review boards of five separate universities/academic medical centers.

Since July of 2006 the Coordinating Center at UHCMC has worked diligently with the Military Operational Medicine Research Program (MOMRP), the U.S. Army Medical Research and Materiel Command, and Institutional Review Boards (IRBs) from UHCMC, UT, and the Ann Arbor VA to ensure that this important study is conducted in accordance with the rules and regulations that govern human subjects research.

The protocols, consent forms, and other study documents are currently in the final stages of regulatory review and approval. Initial local IRB approvals were obtained during the summer 2007 from UHCMC's and UT's IRBs for the Main Project, and the Ann Arbor VA's IRB for the Genetics Study. From August 2007 to March 2008, the Coordinating Center was working with MOMRP's Office of Research Protection (ORP) to review and amend the study documents. ORP gave approval for the sites to submit the amended documents to the local IRBs in March 2008, and since then UT's IRB has approved the amendment for the main project, the Ann Arbor VA has approved the

amendment for the Genetics Study, and UHCMC's IRB is still reviewing the amendment for the main project. The UHCMC IRB will review the Genetics Study after the main project is approved. It is anticipated that active enrollment into both the primary project will commence during the summer of 2008 (see attached timeline), with the Year 1 interviews to be completed within 12 months of the project opening for enrollment.

In addition to approval by the U.S. Army Medical Research and Materiel Command, Military Operational Medicine Research Program, the project is fully supported by the leadership of the Ohio National Guard (see ONG letter of support in Appendix). Dr. Calabrese is an extremely active member of the Ohio National Guard-sponsored OHIOCARES Workgroup, and has served as Chairman of the Provider Issues Committee and is a member of the Sub-Committee on Quality Improvement, Tricare Healthcare for the Reserve Component.

This ongoing research project has been designed to function as a template, upon which other projects, will be superimposed. The Office of Research Protections of the MOMRP and the IRB's of record have given permission to re-contact previously studied participants and their family members for the proposed study of neuroanatomical determinants of resilience using neuroimaging methodology.

In March 2008, a conference call was held with the Ohio National Guard and the investigative team regarding operational details for the main project alert letter mailing. LTC Jane Lengel, the Coordinator of OHIOCARES Workgroup, has been very helpful and assisted in all relevant aspects of the project.

A similar conference call was held in April 2008 amongst the investigative team to finalize the operational details for the Genetics Study, which has led to minor changes in the Alert Letter and a significant shortening of the telephone survey battery to minimize service member burden.

Key Research Accomplishments

The key accomplishments of this project to date focus on the establishment of solid, mutually beneficial working relationships with the leadership of the Ohio National Guard (including COL John Harris and Adjutant General Wayt) and the creation of a six site research infrastructure necessary to carry out the projects short-and long-term objectives.

Reportable Outcomes

Not applicable as project has not started enrollment to date.

Conclusion

1. This project is not requesting any changes in its aims or long-term objectives.
2. This project will provide the military with novel, landmark long-term, prospective data that will elucidate novel predictors of resilience to combat-related stress. Compared to existing research in this area, this project is unique because it is population-based and does not limit its scope of study to only VA-treatment seeking veterans. Accordingly, this study is likely to uncover rates of PTSD and other mental conditions following combat that differ from those found in previous scientific reports.

References

Not applicable

Appendices

Letter of support from the Adjutant General of the Ohio National Guard.

STATE OF OHIO
ADJUTANT GENERAL'S DEPARTMENT
2825 West Dublin Granville Road
Columbus, Ohio 43235-2789

August 17, 2007

Director of Personnel

Dr. Joseph Calabrese
Dr. Marijo Tamburrino
Mood Disorders Program
Intervention and Services Research
University Hospitals Case Medical Center
11400 Euclid Avenue, Suite 200
Cleveland, Ohio 44106

Dear Dr. Calabrese and Dr. Tamburrino:

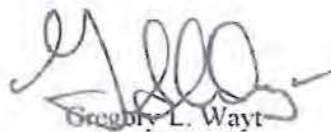
The Ohio National Guard (ONG) is pleased to participate in the "Risk and Resilience" project being conducted by Case Western Reserve University (CWRU). This research project will collect data to quantify the prevalence of post traumatic stress disorder and improve treatment for our service members.

The U.S. Army Medical Research and Materiel Command recommended the project for funding, and COL Craig L. Urbauer, Chief Surgeon at National Guard Bureau, has approved the project. Additionally, the ONG reviewed the "Risk and Resilience" project and determined it meets all the requirements outlined in NGB memorandum, *Human Subject Research Involving National Guard Personnel as Subjects*, dated 14 September 2006.

Under the Privacy Act of 1974, 5 USC 552a, the ONG cannot release any National Guard member's personal information without the express consent of the National Guard member. To assist CWRU in the initial mailing, the ONG will affix mailing labels to postpaid envelopes provided by CWRU.

The "Risk and Resilience" research project will bring future benefits for the mental health care needs of our service members, and the ONG is pleased to participate in this worthy endeavor.

Sincerely,



Gregory L. Wayt
Major General
The Adjutant General